REMARKS/ARGUMENTS

Applicants acknowledge receipt of the Office Action mailed from the United States Patent Office on January 19, 2006. Claim 2 was previously cancelled. Of the remaining claims 1 and 3-77, claims 1, 3, 14-16, 25-35, 37, 40, 46-50, 52-54, 56, 58, 66, and 68 are pending in the application. Of these the Examiner states that claims 15-16, 30-35, 37, 40, 46-48, 50, 52-54, 58 and 68 are deemed allowable, but objected to for being dependent upon a rejected base claim. Claims 4-13, 17-24, 36, 38-39, 41-45, 51, 55, 57, 59-65, 67, and 69-77 were previously withdrawn, but are dependent upon claim 1. Thus, applicants respectfully request rejoinder upon allowance of claim 1.

Rejection under 35 U.S.C.§102(b)

Claims 1, 3, 14, 25-29, 49, 56 and 66 were rejected as being anticipated by Swanson et al. (Swanson, S.J., et al. *The Plant Cell*, May 1998, 10, 685-698) as evidenced by Ozkan et al. (Ozkan et al. *Biochim. Biophys. Acta.* 2002, 1572, 143-148).

The examiner's position is that Swanson et al. disclose the use of a library of fluorescent conjugates in screening and/or characterizing two forms of vacuoles, protein storage and secondary vacuoles. The examiner specifically refers to BCECF-AM and ZFR-CMAC-GS in the the abstract and Table 1 of Swanson et al as examples of the complexes used to identify the vacuole as a secondary or a protein storage vacuole.

The present claims are directed to a method of screening for a substrate to a transport protein by providing a library of different complexes, the complexes have a compound (a test substrate) and a reporter. When the reporter is a fluorophore, the complex also includes a quencher. The substrate-reporter complex (with quencher, if present) is contacted with cells expressing carrier type proteins, and a signal is detected when the complex is internalized in the cell. This indicates that the test substrate is a substrate for at least one carrier-type protein.

Swanson et al. discusses the use of a number of fluorescent compounds in screening and/or characterizing two forms of vacuoles, protein storage and secondary vacuoles. Table 1 of Swanson et al. sets out all of the compounds used for characterization of vacuoles. The compounds are listed in groups by the location of fluorescence (cytoplasm and/or vacuole). All

of the compounds used were fluorescent compounds. In most cases, they were only fluorescent reporters. One was a fluorescent reporter-quencher complex (BCECF-AM) and only one could arguably be called a fluorescent reporter-quencher-substrate complex (ZFR-CMAC-GS) because a glutathione (GS) substrate was added intracellularly.

> In order to be an anticipatory reference, the single reference cited by the Office must disclose each and every element of the claims. *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81 (Fed. Cir. 1986).
> Swanson et al. does not disclose all of the claim elements for the following reasons.

1. Swanson et al. does not teach or disclose the step of "providing a library comprising different complexes, each complex comprising a compound and a reporter, the compound varying between different complexes;" because only one complex as claimed is discussed in Swanson et al.

All of the reporters discussed in Swanson et al. are fluorophores (see Table 1 for a summary). For this reason, to fit the definition of a complex as claimed, Swanson et al would need to disclose a substrate-reporter-quencher complex. The examiner specifically refers to two complexes that are dislosed by Swanson et al., BCECF-AM and ZFR-CMAC-GS and states that these complexes constitute a library. However, in fact BCECF-AM is not a complex as defined in the claims because it does not include a substrate. BCECF-AM is simply a reporter/quencher complex. Assuming aguendo that ZFR-CMAC-GS does fit the definition of a complex, it is the only complex disclosed in Swanson et al. as claimed. The rest of the fluorophores are presented in Table 1 and are simply fluorophores. They do not contain either substrates or quenchers. Therefore, Swanson et al. at most discuss one complex and does not provide a "library comprising different complexes."

2. Swanson et al. does not teach or disclose the step of "contacting the population of cells with a plurality of complexes from the library" because the only complex that Swanson discusses that arguably fits the claimed definition is produced intracellularly. The cells are not contacted with complex because the complex is not formed until the reporter/quencher agent enters the cell.

The intracellular formation of ZFR-CMAC-GS is shown on page 690 and in Figures 4 and 5 of Swanson et al. ZFR-CMAC-GS, includes ZFR as a quencher, CMAC as a reporter, and

GS (glutathione) as a substrate for one type of transport protein found on vacuole membranes (tonoplasts). However, the substrate glutathione (GS) is added intracellularly. This is stated on page 690 column 1, 2nd paragraph as follows, "Probes such as ZFR-CMAC (Figures 4 and 5)....are transported across the tonoplast of isolated vacuoles after conjugation to glutathione." and is shown in Figure 4 where glutathione is added after the ZFR-CMAC enters the cell by an enzyme, GST. The ZFR-CMAC-GS then enters the vacuole by binding to a specific transporter that requires the addition of GS. Thus, the method in Swanson et al does not involve "contacting the population of cells with a" complex.

For the above reasons, Swanson et al. does not disclose all of the claim elements and Swanson et al. does not anticipate the claimed invention.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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